REMARKS

Applicants respectfully requests entry of the amendments and remarks submitted herein. Claims 9-10, 16 and 22 are amended, claims 1-6, 11 and 23-24 are canceled, and claims 29-32 are added. Therefore, claims 7-10, 12-22 and 25-32 are currently pending, with claims 9-10, 12-16, 25-26 and 28-32 under active examination.

Specification Informalities

The Examiner has objected to the disclosure because it contains an embedded hyperlink. Applicant has amended the specification to delete the hyperlinks, and requests that this objection be withdrawn.

Rejection under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 10 and 12-16 (vaccine composition) are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner indicates that claims 10 and 12-16 are "vaccine compositions." It appears that the Examiner erroneously listed claim 10 in this "vaccine" group along with claims 12-16, as claim 10 does not recite a vaccine. Therefore, this rejection should not apply to claim 10.

With respect to claims 12-16, Applicant hereby traverses this rejection. Claim 12 recites a vaccine comprising an immunogenic amount of an isolated and purified polypeptide comprising phospholipase D from *Neisseria gonorrhoeae*, wherein the polypeptide comprises SEQ ID NO:14, which amount is effective to immunize a patient against a neisserial infection of cervical cells, in combination with a physiologically-acceptable, non-toxic vehicle. Claims 13-16 depend from claim 12.

Page 5 of the Office Action states that "[t]he specification on pages 68-78 recite that the antibodies to CR3, CD18 inhibit the binding of Neisseria to cervical epithelial cells. However, as the claimed protein comprising the amino acid sequence SEQ.ID.NO:14 (strains, MS11 and strain 1291, encoding secretion system) would directly inhibit the infectivity has not been shown." It should be noted, however, that Applicant is not claiming that the PLD protein (SEQ

ID NO:14) directly inhibits the infectivity of *Neisseria*. Claim 12 recites a vaccine comprising an immunogenic amount of the PLD protein (SEQ ID NO:14), which amount is effective to immunize a patient against a neisserial infection of cervical cells, in combination with a physiologically-acceptable, non-toxic vehicle. Thus, the PLD is a vaccine (i.e., a composition effective in raising an immune response and/or effective in inducing the generation of antibodies) that inhibits neisserial infectivity; the PLD itself is not inhibiting the neisserial infectivity.

The Examiner alleges that Applicant has not disclosed that the claimed isolated and purified polypeptide comprising the amino acid sequence as set forth in SEQ ID NO:14 or an isolated polypeptide encoded by the nucleic acid sequence SEQ ID NO:13 would effectively prevent, ameliorate, or reduce the incidence of all *N. gonorrhoeae* strains in an established ex vivo model system.

It is well established that there is no art-accepted animal model for human gonococcal infection, even though researchers have attempted to generate an effective animal model for the disease. See, for example, the Cohen and Cannon reference (*J. Infect. Dis.* (1999) 179 (Suppl. 2):S375-S379), which teaches that there is no valid experimental animal model that might be useful to develop a gonorrhea vaccine. This reference also discloses that experimental gonorrhea cannot be pursued in women due to the likelihood of complications. Since experimental gonorrhea cannot be studied in women, primary cervical cells are an art-accepted system in which to evaluate the potential immunogenic use of *N. gonorrhoeae* proteins. Primary cervical cells are an established *ex vivo* model system for evaluating gonococcal infection, and have been used to generate data that is sufficient to support the present claims.

Applicant has shown in Example 8 of the specification that anti-PLD sera (Ab 1307) could be generated, and that the anti-PLD sera was found to inhibit PLD activity and the association and invasion of cervical cells by gonococci. Applicant performed further studies where various strains of *N. gonorrhea* were prevented from associating with cultured primary cervical cells in the presence of Ab 1307. (*See*, Declaration of Dr. Apicella under 37 C.F.R. § 1.132 dated September 25, 2006.) In addition to strain 1291, three other clinical gonococci isolates/strains were used to challenge primary cervical cells. One strain was a cervical isolate ("cervical") (strain LT38097), one was from a patient with pelvic inflammatory disease ("PID") (strain PID6), and one strain was from a patient with disseminated gonococcal infection ("DGI")

(SK92-679). The association/invasion assays were performed with or without anti-PLD Ab 1307. As can be seen from the data, presence of Ab 1307 effectively inhibited the ability of various neisserial strains from invading the cells. Thus, these experiments establish that anti-PLD antibodies provide protective immunity by interfering with gonococcal infection. As such, Applicant's use of this *ex vivo* model system clearly provides support for the effectiveness of using PLD as a vaccine to provide protective immunity by interfering with gonococcal infection.

The Examiner further states that the specification has not disclosed a link or nexus between the generation of protective immunity and the claimed polypeptide. As discussed above, Applicant has shown that PLD is an effective antigen, *i.e.*, that it can induce the production of anti-PLD antibodies. Applicant has also shown that the presence of anti-PLD antibodies effectively inhibited the ability of various neisserial strains from invading cells. Thus, Applicant has shown a nexus between the claimed PLD protein and the generation of protective immunity against several strains of *N. gonorrhoeae*.

The Examiner also states that there is no objective basis upon which the skilled artisan would reasonably be able to determine or predict an amount of the claimed vaccine effective for its intended use. Applicants also submit that the teachings of the specification, in combination with the level of skill in the art at the time the application was filed, would have enabled the use of the claimed polypeptides in vaccines against neisserial colonization. Applicants respectfully submit that the relative skill of those in the art at the time the application was filed can be characterized as being quite high. Those skilled in the art at the time Applicants filed the present application can be considered scientists who understood the problems associated with human infection by *N. gonorrhoeae*, the lack of a suitable animal model, and the vast possibilities for immunization against *N. gonorrhoeae* once a suitable immunogen was identified. Clearly, a person skilled in the art would have been well aware of the types of experiments needed to determine whether a neisserial polypeptide such as PLD would be useful in a vaccine to immunize a subject against gonorrhea. For example, Applicants submit that a person of skill in the art would have been able to perform well-known biochemistry, molecular biology, and/or immunology techniques such as recombinant protein expression, protein purification, and generation and characterization of antibodies. A person of skill in the art also would have been able to determine a suitable dose of vaccine to administer to a particular subject. Thus, Applicants respectfully submit that given the teachings of the specification and the level of skill

in the art, a person having ordinary skill in the art, reading Applicants' specification at the time the application was filed, would have been able to make and use the presently claimed vaccine without undue experimentation. Specific dosage amounts are not disclosed and, Applicants submit, are not required, since amounts will vary depending on the route of administration, and the age and condition of the recipient (see specification at page 52, lines 19-27).

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 10, and 2-16 under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claims 9, 10, 11, 25, 26, and 28 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention.

Claim 9 is rejected as being vague for the recitation of "nucleic acid sequence SEQ ID NO:9, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19 or SEQ ID NO:32" because applicant's election is drawn to an isolated and purified polypeptide comprising the amino acid sequence SEQ ID NO:14. The examiner suggests that the claim be amended to recite "an isolated and purified polypeptide comprising the amino acid sequence SEQ ID NO:14 encoded by the nucleic acid sequence SEQ ID NO:13." Claim 9 has been amended as suggested. Applicant requests that this rejection under 35 U.S.C. § 112 be withdrawn.

Claim 10 is rejected as being vague for the recitation of "comprising phospholipase D." Claims 25, 26 and 28 depend from claim 10. The examiner would like clarification that this term refers to an isolated and purified phospholipase D polypeptide from *Neisseria gonorrhea* comprising the amino acid sequence SEQ ID NO:14. Claim 10 has been amended as suggested. Applicant requests that this rejection under 35 U.S.C. § 112 be withdrawn.

Claim 11 is rejected as being vague for the recitation of "comprises SEQ ID NO:4, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18 or SEQ ID NO:20." The examiner would like clarification that applicant is referring to the polypeptide of claim 10, wherein the polypeptide comprises the amino acid sequence SEQ ID NO:14. Claim 11 has been cancelled, thereby rendering this rejection moot.

Rejections under 35 U.S.C. § 102

de la Paz et al.

The Examiner has rejected claims 10-16, 25-26, and 28 under 35 U.S.C. § 102(b) as being anticipated by de la Paz et al. (1995, Microbiology 141:913-920). Claim 11 has been canceled. Insofar as this rejection is applied to the pending claims, it is hereby traversed.

To constitute anticipation, the claimed subject matter must be identically disclosed in the prior art. *In re Arkley*, 172 U.S.P.Q. 524 at 526 (C.C.P.A. 1972). For anticipation, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the art. *Scripps Clinic & Res. Found. v. Genenteh, Inc.*, 927 F.2d 1565, 18 U.S.P.Q.2d 101 (Fed. Cir. 1991).

De la Paz et al. disclose outer-membrane proteins (OMP) from *N. gonorrhoeae* strain p9. The Examiner alleges at page 7, section 13 of the Office Action that "Outer membrane proteins (OMP) from *N. gonorrhoeae* would inherently contain the claimed protein and several other proteins that are linked together." Applicant respectfully disagrees with this allegation. The fraction OMP would not necessarily contain the claimed protein (PLD), if the claimed protein were a secreted protein. PLD is not an OMP. PLD is a secreted protein (specification at page 93, lines 18-19).

Further, de la Paz et al. do not teach or suggest a purified PLD, nor SEQ ID NO:14, as recited by the pending claims. Therefore, de la Paz et al. do not teach or suggest the claimed invention.

Thus, the examiner is requested to withdraw the rejection of claims 10, 13-16, 25-26, and 28 as being anticipated under 35 U.S.C. § 102(b) by de la Paz et al.

Fraser et al.

The Examiner has rejected claims 9-16, 25-26, and 28 under 35 U.S.C. § 102(b) as being anticipated by Fraser et al. (1999) Accession Number AAY 75751 (cited in WO 99/57280 as SEQ ID NO:2974) or AAY 75753 (cited in WO 99/57280 as SEQ ID NO:2978). The Examiner states that WO 99/57280 discloses that the polypeptides could be used as a vaccine, an immunogenic composition, or to raise antibodies. Thus, the Examiner concluded that WO 99/57280 anticipates the presently claimed invention.

Applicant respectfully asserts that WO 99/57280 does not disclose all of the features of the present amended claims. WO 99/57280 provides 3,020 nucleic and amino acid sequences corresponding to 999 possible ORFs. This reference also presents computer analyses of these sequences, including the determination of putative amino acid sequences than might be encoded by deduced open reading frames. At pages 1393-1394, WO 99/57280 sets forth a partial DNA sequence identified in *N. gonorrhoeae* (SEQ ID NO:2973). The amino acid sequence that corresponds to this partial DNA sequence is set forth on page 1394 (SEQ ID NO:2974), which is part of what was designated "ORF 987." At page 1396, WO 99/57280 sets forth a partial DNA sequence identified in *N. meningitidis* (SEQ ID NO:2977). The amino acid sequence that corresponds to this partial DNA sequence is set forth on pages 1396-1397 (SEQ ID NO:2978), which is part of what was designated "ORF 2978."

WO 99/57280 provides a description of several generally-known expression systems at pages 59-66. WO 99/57280 teaches the expression of the following ORFs from *N. meningitidis* using know expression systems:

ORF 919 (Example 2, pages 111-112 and page 1320),
ORF 279 (Example 3, page 112 and page 635),
ORF 576 and 576-1 (Example 4, pages 112-113 and page 893),
ORF 519 and 519-1 (Example 5, page 113 and page 781),
ORF 121 and 121-1 (Example 6, page 114),
ORF 128 and 128-1 (Example 7, pages 114-115),
ORF 206 (Example 8, page 115),
ORF 287 (Example 9, page 116), and
ORF 406 (Example 10, pages 116-117).

WO 99/57280 does not teach the expression of ORF 987 or ORF 2978. WO 99/57280 does not disclose the expression of any polypeptide from *N. gonorrhoeae*, let alone the expression and isolation or purification of polypeptides from *N. gonorrhoeae*.

Applicants assert that WO 99/57280 does not teach the claims as presently amended. WO 99/57280 merely sets forth nucleic acid sequences of possible ORFs that might be translated into putative proteins. Moreover, WO 99/57280 does not disclose purification or isolation of any *N. gonorrhoeae* protein, as recited in the pending claims. As such, WO 99/57280 does not anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of the pending claims under 35 U.S.C. § 102(b) by Fraser et al. (1999) Accession Number AAY 75751 or AAY 75753.

Parkhill et al.

The Examiner has rejected claims 9-16, 25-26, and 28 under 35 U.S.C. § 102(a) as being anticipated by Parkhill et al. (2000, Accession Number B81859). Specifically, the Examiner stated that the Parkhill *et al.* reference discloses a *N. meningitidis* polypeptide with an amino acid sequence that is 97.2% similar to the claimed SEQ ID NO:14. (Later in the paragraph on page 9, the Examiner states that the polypeptide is 100% identical to the claimed polypeptide, which is incorrect.) This polypeptide is encoded by a nucleic acid sequence that is 92.2% identical to the claimed sequence (SEQ ID NO:13). The Examiner further stated that characteristics such as a phospholipase D activity is considered to be an inherent property of the polypeptide disclosed in the Parkhill *et al.* reference. Thus, the Examiner concluded that the Parkhill *et al.* reference anticipates the present invention.

Applicants assert that the Parkhill *et al.* reference does not teach the claims as presently amended. The Parkhill *et al.* reference cited by the Examiner merely sets forth the amino acid sequence of a putative protein. Moreover, the *Nature* article corresponding to the cited Parkhill *et al.* reference merely discloses that the complete genomic sequence of a particular strain of *N. meningitidis* was obtained and compared with sequences in the EMBL database to identify potential open reading frames. Neither of these references discloses purification or isolation of any *N. gonorrhoeae* protein, as recited in the pending claims. Further, the Parkhill *et al.* references fail to disclose the use of the protein in a vaccine as recited in claim 12. As such, the cited Parkhill *et al.* reference does not anticipate the present claims.

In light of the above, Applicants respectfully request withdrawal of the rejection of the pending claims under 35 U.S.C. § 102(a).

CONCLUSION

The Examiner is invited to contact Applicant's Representative at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby. If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3503. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extension fees to Deposit Account 50-3503.

Respectfully submitted,

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